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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

ART UNIT	PAPER NUMBER
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DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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105014
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VAT 7/23/01

Office Action Summary

Application No.

09/554,868

Applicant(s)

Halvorsen

Examiner

Arun Chakrabarti

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Feb 21, 2001
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31-40 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31, 37, 38, and 40 is/are rejected.
- 7) ☒ Claim(s) 32-36 and 39 is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

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DETAILED ACTION

Specification

1. Claims 1-30 have been canceled without prejudice towards further prosecution. New claims 31-40 have been added.

Claim Objections

2. Claims 32-36 and 39 are objected to because of the following informalities: Claims 32-36 and 39 are improperly dependent on a canceled and non-existent claim 1. Appropriate corrections are required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 31, 37-38 and 40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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Claim 31 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for adipose tissue-derived human stromal cells does not reasonably provide enablement for adipose tissue-derived stromal cells from any animal species. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claim. For example, only one adipose tissue-derived human stromal cells has been described in Figure 1.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 32-36 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 32-36 and 39 are rejected because they are dependent on a canceled and non-existent claim 1. The metes and bounds of the claims are vague and indefinite.

Claims 31, 37 and 38 are also rejected over the recitation of the phrase, "adipose stromal cells". It is not clear if the cells are at stem cell stage or competent stem cell stage or adipose precursor cell stage or adipoblast stage. The metes and bounds of the claims are vague and indefinite.

Claims 31 and 40 are rejected over the recitation of the phrase, "characteristic of a non-adipocyte cell lineage". It is not clear if biochemical characteristics are claimed or morphological

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characteristics are claimed or both are claimed. The metes and bounds of the claims are vague and indefinite.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 37 is rejected under 35 U.S.C. 102 (b) as being anticipated by Simpson et al. (U.S. Patent 5,446,143) (August 29, 1995).

Simpson et al teach an isolated adipose tissue-derived stromal cells in combination with a substance (dexamethasone or glucocorticoid) that promotes differentiation (Column 8, line 45 to column 9, line 38 and Table 2 and Figure 3).

9. (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

10. Claims 31, 37 and 40 are rejected under 35 U.S.C. 102 (e) as being anticipated by Katz et al. (U.S. Patent 5,786,207) (July 28, 1998).

Katz et al inherently teach an adherent isolated adipose tissue-derived stromal cell that exhibits at least one characteristic of a non-adipocyte cell lineage (Column 2, lines 19-35). The non-adipocyte cell lineage characteristic is inherently achieved when the cells obtained from

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human liposuction tissues are de-differentiated, culture-expanded and re-differentiated by chemical stimulation as explicitly taught by Katz et al (Column 2, lines 19-35).

Katz et al inherently teach an isolated adipose tissue-derived stromal cells in combination with a substance that promotes differentiation (Column 2, lines 29-35).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 31, 37, 38 and 40 are rejected under 35 U.S.C. 103 (a) over Katz et al. (U.S. Patent 5,786,207) (July 28, 1998) in view of Poliard et al. (The Journal of Cell Biology, (1995), Vol. 130 (6), pages 1461-1472).

Katz et al teach the cells of claims 31, 37 and 40 as described above.

Katz et al do not teach the ascorbic acid or beta-glycerophosphate as the substances that promotes differentiation.

Poliard et al. teach the ascorbic acid or beta-glycerophosphate as the substances that promotes differentiation in competent C1 stem cells which has all the property of adipose stromal cells (Figure 9 and Page 1470, column 1, third paragraph to column 2, second paragraph).

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Poliard et al state, "Under AA and beta-GP culture conditions, C1 cells appear unequivocally committed towards the osteogenic pathway (Page 1462, Column 1, last sentence)."

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the osteogenic differentiation of common stromal cells in presence of beta-glycerophosphate and ascorbic acid as suggested by Poliard et al to form osteoblasts in the adipose tissue-derived cells easily obtained by liposuction that is differentiated in order to exhibit at least one characteristic of a non-adipocyte cell lineage of Katz et al, since Poliard et al. state, "In the adult, there is also evidence that adipogenic or osteogenic cells might derive from a common stromal stem cell of the bone marrow. It also confirms close ontogenic relationship occurring between various members of the skeletal connective tissue family (Page 1470, column 2, Concluding Remarks, last two sentences)". Moreover, Poliard et al state, "Finally, the addition of appropriate inducers is strictly required to turn on one or the other differentiation program. Each inducer acts as an instructive signal since it elicits a temporal regulation of gene expression capable to drive cells to the differentiated endstage (Page 1471, column 1, third paragraph, first two sentences)". By employing scientific reasoning and in order to improve the production of bone-forming osteoblast cells from easily available adipose tissues for treating skeletal and other connective tissue disorders, one ordinary artisan would have combined adipose tissue-derived stromal cells with ascorbic acid or beta-glycerophosphate that promotes differentiation. An ordinary practitioner would have been motivated by the express statements of Poliard et al to substitute and combine the adipose tissue-derived stromal cells that

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is differentiated in order to exhibit at least one characteristic of a non-adipocyte cell lineage of Katz et al in the osteogenic differentiation of common stromal cells in presence of beta-glycerophosphate and ascorbic acid as suggested by Poliard et al to form osteoblasts in order to achieve the express advantages, as noted by Poliard et al., of a method which provides the common tripotent pathway capable of giving rise to either osteocytes, chondrocytes, or adipocytes depending on the addition of appropriate inducers strictly required to turn on one or the other differentiation program, especially under AA and beta-GP culture conditions in which cells appear unequivocally committed towards the osteogenic pathway and also in order to achieve the express advantages, as noted by Katz et al., of manipulating the growth and differentiation of adipocyte precursor cells derived from human adipose tissue.

13. Claims 31, 37, 38 and 40 are rejected under 35 U.S.C. 103 (a) as being obvious over Poliard et al. (The Journal of Cell Biology, (1995), Vol. 130 (6), pages 1461-1472) in view of Caplan et al. (U.S. Patent 5,226,914) (July 13, 1993).

Poliard et al suggest adipogenic cells might be derived from a common stromal stem cells of the bone marrow and the adipose precursors arise from multipotential embryonic stem cells determined to become mesodermal cells. Poliard et al also teach that the adipogenic differentiation of C1 cells resembles that of preadipocyte cell lines and the osteocyte generation from competent C1 stem cells which has all the property of adipose stromal cells depends only on the presence of beta-glycerophosphate and ascorbic acid (Figure 9 and Page 1470, column 1, third paragraph to column 2, second paragraph). Poliard et al state, "Under AA and beta-GP

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culture conditions, C1 cells appear unequivocally committed towards the osteogenic pathway (Page 1462, Column 1, last sentence).”

Poliard et al do not teach adipose tissue-derived stromal cells that is differentiated in order to exhibit at least one characteristic of a non-adipocyte cell lineage e.g., formation of osteoblasts.

Caplan et al teach adipose cells that is differentiated in order to exhibit at least one characteristic of a non-adipocyte cell lineage e.g., formation of connective tissues depending upon the influence of a number of bioactive factors (Column 4, lines 2-9).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the adipose tissue-derived stromal cells that is differentiated in order to exhibit at least one characteristic of a non-adipocyte cell lineage of Caplan et al in the osteogenic differentiation of common stromal cells in presence of beta-glycerophosphate and ascorbic acid as suggested by Poliard et al to form osteoblasts since Poliard et al. state, “In the adult, there is also evidence that adipogenic or osteogenic cells might derive from a common stromal stem cell of the bone marrow. It also confirms close ontogenic relationship occurring between various members of the skeletal connective tissue family (Page 1470, column 2, Concluding Remarks, last two sentences)”. Moreover, Poliard et al state, “Finally, the addition of appropriate inducers is strictly required to turn on one or the other differentiation program. Each inducer acts as an instructive signal since it elicits a temporal regulation of gene expression capable to drive cells to the differentiated endstage (Page 1471,

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column 1, third paragraph, first two sentences)". Further motivation is provided by Caplan et al, as Caplan et al state, "However, the mesenchymal stem cells are present in the tissue not only in very minute amounts with a wide variety of other cells (i.e., erythrocytes, platelets, neutrophils, lymphocytes, monocytes, eosinophil, basophil, adipose cells, etc.) in an inverse relationship with age, they are capable of differentiating into an assortment of connective tissues depending upon the influence of a number of bioactive factors (Column 4, lines 2-9)". By employing scientific reasoning and in order to improve the production of bone-forming osteoblast cells from easily available adipose tissues for treating skeletal and other connective tissue disorders, one ordinary artisan would have combined adipose tissue-derived stromal cells with several substances that promotes differentiation. An ordinary practitioner would have been motivated by the express statements of Poliard et al to substitute and combine the adipose tissue-derived stromal cells that is differentiated in order to exhibit at least one characteristic of a non-adipocyte cell lineage of Caplan et al in the osteogenic differentiation of common stromal cells in presence of beta-glycerophosphate and ascorbic acid as suggested by Poliard et al to form osteoblasts in order to achieve the express advantages, as noted by Poliard et al., of a method which provides the common tripotent pathway capable of giving rise to either osteocytes, chondrocytes, or adipocytes depending on the addition of appropriate inducers strictly required to turn on one or the other differentiation program, especially under AA and beta-GP culture conditions in which cells appear unequivocally committed towards the osteogenic pathway and also in order to

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achieve the express advantages, as noted by Caplan et al., of differentiating adipose cells into an assortment of connective tissues depending upon the influence of a number of bioactive factors.

Conclusion

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Chakrabarti

Arun Chakrabarti
Patent Examiner
Art Unit 1655,
April 24, 2001

Jeffrey Fredman
JEFFREY FREDMAN
PRIMARY EXAMINER

Notice of References Cited

Applicant/Patent

Halvorsen

Application/Control No.

09/554,868

Examiner

Arun Chakrabarti

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U.S. PATENT DOCUMENTS

	Document Number <small>Country Code-Number-Kind Code</small>	Date <small>MM-YYYY¹</small>	Name	Classification ²	
A	5,786,207	7/1998	Katz et al.	435	267
B	5,446,143	8/1995	Simpson et al.	536	24.1
C	5,226,914	7/1993	Caplan et al.	623	16
D					
E					
F					
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I					
J					
K					
L					
M					

FOREIGN PATENT DOCUMENTS

	Document Number <small>Country Code-Number-Kind Code</small>	Date <small>MM-YYYY¹</small>	Country	Name	Classification ²	
N						
O						
P						
Q						
R						
S						
T						

NON-PATENT DOCUMENTS

	Include, as applicable: Author, Title, Date, Publisher, Edition or Volume, Pertinent Pages
U	Poliard et al., "Controlled conversion of an immortalized Mesodermal Progenitor Cell Towards Osteogenic, Chondrogenic or Adipogenic Pathways", <i>The Journal of Cell Biology</i> , Vol. 130, No. 6, pages 1461-1472., July 13, 1993.
V	
W	
X	

* A copy of this reference is not being furnished with this Office action. See MPEP § 707.05(a).

¹ Dates in MM-YYYY format are publication dates.

² Classifications may be U.S. or foreign.